Universitat Autònoma de Barcelona

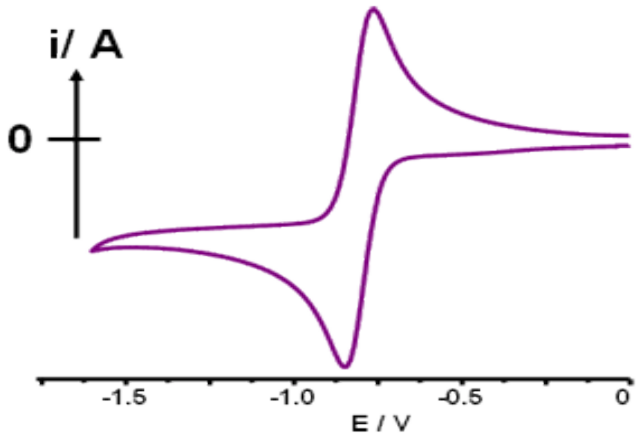
Electrochemically promoted carbon-halide bond cleavage in 4-nitrobenzyl halides

Màster Universitari Ciència i tecnologia químiques

Mòdul d'Iniciació a la recerca i treball fi de master

Departament de química

Facultat de Ciències



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Bellaterra, September 1, 2011

Acknowledgment

First of all, I would like to express my deepest sense of gratitude to my supervisor Dr. Iluminada Gallardo for the encouragement and excellent advice throughout this study. I am thankful to Dr. Gonzalo Guirado for his generous assistance and his patient guidance during this time.

My family is the most amazing thing that I have in my life. They encourage me to be a better human being. The want the best for my and they do anything to help me to reach my goals.

Madeline, Lyma and Martin are the best friends that any person can have. I know they are always be there for me. The internet is the best thing we have, go messenger!!!!!!!! Our virtual party's are the best!!!!!

Luis, there is not words to describe how much you help me and much I love you. Thanks for believe in me and encourage me to have confidence.

Abstract

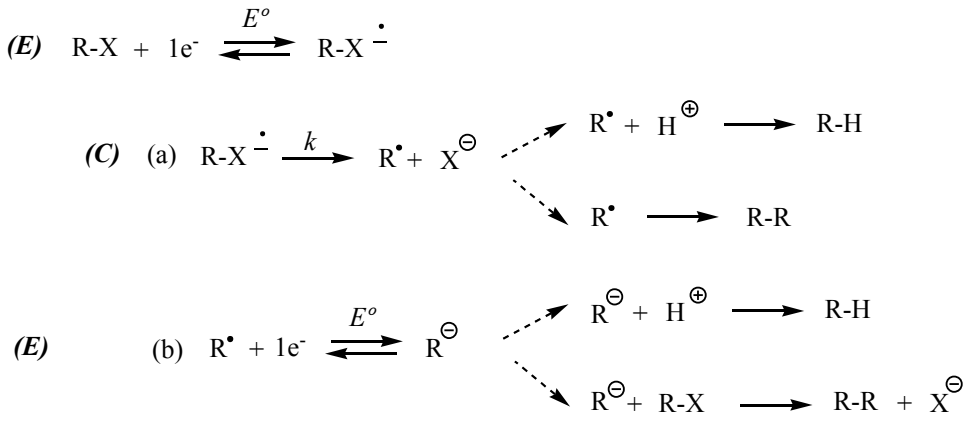
This manuscript reports the study of the carbon-halide bond cleavage in 4-nitrobenzyl halides, taking special attention to the iodide and fluoride derivatives. The electrochemical reduction mechanism has been disclosed for both compounds by terms of cyclic voltammetry and controlled potential electrolysis. In the case of 4-nitrobenzyl iodide, a first one electron irreversible wave leads to the corresponding 4-nitrobenzyl radical and iodide. However, in the case of 4-nitrobenzyl fluoride, a first one-electron reversible wave appears at –1.02 vs. SCE followed by one electron irreversible wave. In this second electron transfer process, the cleavage of the C-F bond is taking place, so the bond cleavage reaction occurs at the dianion level. To disclose and understand the electrochemical reduction mechanisms that allows to obtain important thermodynamic and kinetic data that would help in the understanding of C-X bond cleavage. This type of bond dissociation reactions are involved in the metabolism pathways of the human body.

Table of Contents

Introduction

Electrochemical processes in which chemical reactions accompany the initial transfer of one electron is actually a pretty common situation in organic reactions, since the radical or ion radical species resulting from this initial step are very often chemically unstable. In this reactions the first electron transfer of the intermediate, so its reduction (or oxidation), is performed at the electrode. However, the second electron transfer if there is one, which will be usually energetically more costly than the first, can occur either in the electrode surface or in solution[1]. When these two processes take place at successive values of the electrode potential (EE mechanism, where E means electrochemical step), there is therefore no difficulty of preventing the occurrence of the second reaction by an appropriate adjustment of the electrode potential.

At the level of the first electron transfer, the reactions affecting the initially formed intermediate fall into two categories unimolecular reactions and bimolecular reactions. The first category involves single electron transfer to or from molecules is often accompanied by other reactions involving bond formation and/or cleavage[2]. When the reaction accompanying electron transfer is a bond breaking, a free radical and a diamagnetic leaving group may be produced via single electron transfer to a diamagnetic molecule. The resulting high-energy radical intermediate can follow two reaction pathways: a) it reacts with the solvent (H-atom abstraction) or with another radical specie (dimerization) or b) it undergoes further electron transfer with the same electron source or in solution[3]. The result in the first case, a, is a global exchange of one electron per molecule 'EC mechanism' (where E indicates electrochemical step, whereas C chemical step). In the second case, b, since second intermediate formed is easier to reduced (or to oxidize) than the first[2], the result is a global exchange of two electrons per molecule, which occurs in a stepwise manner according to an 'ECE' (i.e., electrochemical-chemical-electrochemical steps) mechanism (Scheme 1).



Scheme 1

The second categories (bimolecular reactions), will involve the dimerization reaction of two anion radicals formed upon a first electron transfer.[1] This mechanism is depicted in Scheme 2, involving, as first follow-up reaction, the coupling of two radical anions. According to the nature of the electron transfer step and the coupled homogenous reaction, which is assumed to be second order, an EC_2 mechanism is operating in this case.

$$\textbf{(E)} \quad \text{R-X} + 1e^- \overset{E^o}{\rightleftharpoons} \text{R-X}^{\bullet -}$$

$$\textbf{(C}_\textbf{2}\textbf{)} \quad 2\ \text{R-X}^{\bullet -} \xrightarrow{k} \text{R-R} + 2\ \text{X}^{\ominus}$$

Scheme 2

The way in which coupled homogeneous reactions can be characterized in terms of mechanism and rate constants by their interference in the electrochemical responses is disclosed usually by cyclic voltammetry. The products formed in preparative-scale electrolysis are an important objective not only for investigating the reaction mechanism in cases where cyclic voltammetry are able to give only a part of it, but also for optimization strategies in the synthesis of the desired products. After the primary radical has evolved through bond breaking reaction upon a first reductive electron transfer (at the anion radical level), the determination of the redox properties of the second radical formed, which is often easier to reduce than the starting molecule, is a challenging task. Combining mechanistic, thermodynamic and kinetic information thus gathered on the formation and reduction of these primary (anion radicals) as well as secondary radicals, allow one to define the conditions under which electrochemistry may trigger either a radical chemistry or an ionic chemistry.

Organohalogens form a large class of organic compounds, which contain halogen substituents. Their discovery and application has benefited numerous important fields. For example: in agriculture, a variety of halogenated pesticides are used to protect crops from infestation; in disease control, DDT has saved millions of lives by controlling the mosquito vector of the deadly disease malaria. This compounds are used in the industrial chemical synthesis, numerous organohalogens serve as important solvents as well as precursors for creating more complex and biologically active compounds[4].

Focusing on unimolecular fragmentation of organic non-aromatic halides Von Stackelberg et al.[3] investigated a large number of compounds by polarography and by controlled potential electrolysis, and were able to formulate the following of useful generalizations.

2 Electrochemically promoted carbon-halide bond cleavage in 4-nitrobenzyl halides

1. Allylic benzylic halides are easy to reduce than the corresponding halides; for example allyl bromide has E^0= -1.29 V vs. SCE in 75 % dioxane containing tetraethylammonium bromide, while under the same conditions n-butyl bromide has E^0 = -2.27 V vs. SCE.
2. Vinyl halides are more difficult to reduce than saturated halides (half-wave potentials of -2.47 and -2.09 V for vinyl and ethyl bromide respectively).
3. Geminal and vicinal polyhalides are easier to reduce than simple halides. For example, one observes the following orders of decreasing ease of reduction: CCl_4>$CHCl_3$>CH_2Cl_2>CH_3Cl.
4. An increase length of the aliphatic chain attached to a carbon atom decreases the ease of reduction: methyl bromide > n-butyl bromide >n-octyl bromide. This is probably an adsorption effect.
5. Half wave potentials are pH independent in R-X compounds. This indicates that the proton transfer cannot occur either, before or in the transition state reduction.

Similar types of studies were reported for aryl halides derivates. It is important to highlighted that in most of the cases the reduction potential value are higher than -2.00 V vs. SCE (Table 1), which makes hardly difficult to perform any kind of mechanistic investigations under this experimental conditions. Note that the cathodic electrochemical window in common electrochemical aprotic solvents (i.e. acetonitrile or dimethylformamide) containing 0.1 M of supporting electrolyte, which are usually tetraalkylammonium salts (i.e. 0.1 M of tetrabutylammonium fluoride), is close to -3.00 V.

Table 1: Reduction potentials of the halonitrobenzenes and related compounds

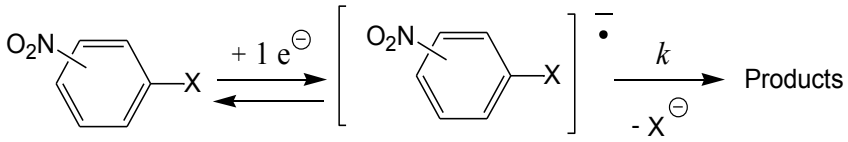
Substrate	E vs. SCE
Iodobenzene	-1.62
Bromobenzene	-2.38
Chlorobenzene	-2.58
Nitrobenzene	-1.18
p-iodonitrobenzene	-1.09
p-bromonitrobenzene	-1.15
p-chloronitrobenzene	-1.08

In order to solved this problem an electrophore group, which must be an electron withdrawing group (EWG) (i.e. NO_2, CN, CF_3), will diminish the reduction potential being this group the initial acceptor of the electron[5]. The presence of a nitro group in the molecule diminishes the reduction potential value at least in 1.4 V (Table 1), being the electrochemical experimental conditions more approachable, and making possible to get more reliable data.

In the case of those nitroaromatic halides, it has been suggested that reduction of certain unsaturated and aromatic halides involves an initial addition of the electron to the π system, followed by cleavage of the sigma bond to halogen. Several authors, including Andrieux et.alt.[6], have proposed that cleavage of C-X bonds in halogeno-aromatic radical anions may be seen as the result of electron transfer from the π radical anion to the σ-arylnucleofugal bond by an orbital crossing. Therefore the complete process would consist of the addition of an electron to an electrophore of a complex molecule, followed by intra-molecular electron transfer, and the subsequent reaction of another part of the molecule. This behavior has been recognized for a number of years as being characteristic of the halonitrobenzenes, for example, for the 4-nitrocompounds in acetonitrile[7-8].

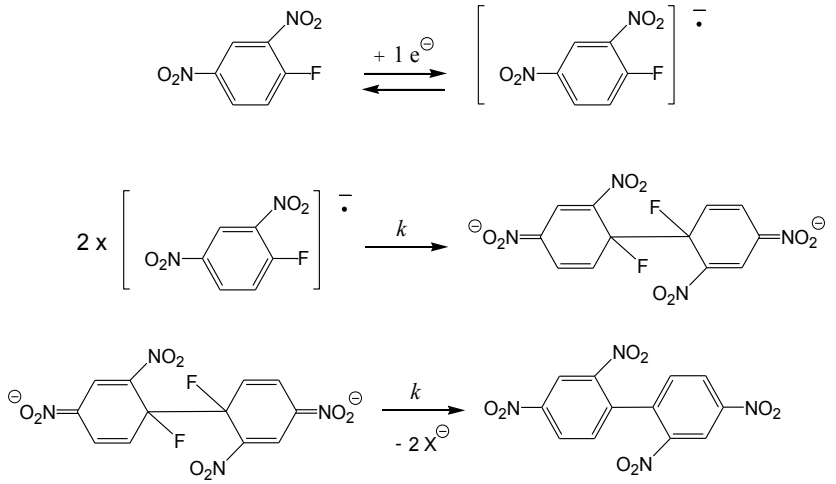
Cyclic voltammetric experiments have demonstrated that: (a) the nitroaromatic electrophore is undoubtedly the initial electron acceptor; (b) the carbon-halogen bond cleavage represented by k_1 formally represents a transference of the added electron from the π system to the orthogonal sigma system and (c) the decomposition rate k_1 depends on X, the order of the halogen mobility being F < Cl < Br < I.[3] It is know from ESR experiments, that there is some coupling between the two systems[9-10], and this coupling presumably provides the mechanism by which bond cleavage takes place.

The nitro group acts as an intramolecular catalyst for removal of the halogen atom. Other examples of this behavior have been recognized in the electrochemical reduction of bromotriphenylethylene[11], haloanthracenes[12], halobenzophenones[13], halobenzonitriles[8] and nitrobenzyl[14] (Scheme 3).



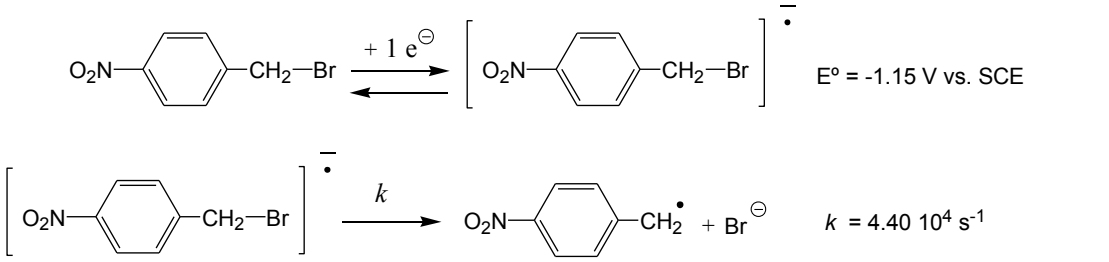
Scheme 3

On the other hand, dimerisation of radical anions prior to C – F bond fragmentation has been postulated in some examples with relatively stable fluorine-substituted radical anions: fluorobenzonitrile[15], pentafluoronitrobenzene[16] and 1-Fluoro-2,4-dinitrobenzene[17] (Scheme 4).



Scheme 4

Finally, in the case of the electrochemical reduction of nitrobenzyl chloride and bromide, which was firstly investigated by Hawley's[7] , Savéant's groups[18], and recently revisited in our research group[19] due to the controversy of those previous studies. It can be concluded that the reduction of the p-nitrobenzyl bromide involves a first heterogeneous electron transfer (-1.00 V vs. SCE), followed by the cleavage of the carbon-halide bond (C-Br) yielding the corresponding nitrobenzyl radical and halide anion. The electrochemical mechanism showed a one electron reduction wave for the p-isomer, which means that the radical formed upon the cleavage of the C-Br bond are relatively persistent ("stable") at these potentials. By using cyclic voltammetry, spectro-electrochemistry and controlled-potential electrolysis together, it was possible to estimate the reduction potential of the nitrobenzyl radical (-1.68 V vs. SCE). The nature of the reduction products yielded after the electrolysis process in function of the applied potential is strongly related with the evolution of the radical. For the p-nitrobenzyl bromide, since the experimental observation is an exchange of one-electron per molecule, the benzyl radical formed upon reduction of the starting material lead to a dimer (radical-radical coupling) or abstract a hydrogen atom from the DMF (Scheme 5). Whereas when the radical is reduced to the anion two electrons are required and the major reaction detected is the protonation of the anion, although a S_N attack from the benzyl anion on the substrate can occur since there is a substantial amount of dimer in the case of the *p*- and *o*- isomers. From a synthetic point of view, the radical-radical dimerisation or the nucleophilic substitution reactions (S_N) from the electrogenerated radicals or anions can be relevant in the design of new environmentally friendly methods of obtaining nitrobenzyl compounds. Taking into account the above mentioned premises the main goals of the current work are presented in the next point.



Scheme 5

Objectives

1. To investigate the electrochemical reduction mechanism of two new nitrobenzyl halides, the 4-nitrobenzyl iodide and 4-nitrobenzyl fluoride, by terms of cyclic voltammetry and controlled potential electrolysis.
2. To disclose the electrochemical reduction mechanism of both compounds by combination of thermodynamic and kinetic information.
3. To establish the main important factors in the kinetics of the dissociative electron transfer reaction of those compounds.
4. To compare the data obtained with the previous data published in the literature for the other nitrobenzyl halide derivatives.

Experimental section

Materials

Solvents

1. Anhydrous *N,N*-dimethylformamide (DMF) is stored in an inert atmosphere with molecular sieves.
2. Toluene, SDS > 99.8 %
3. Dicholromethane (DCM), SDS > 99.8 %

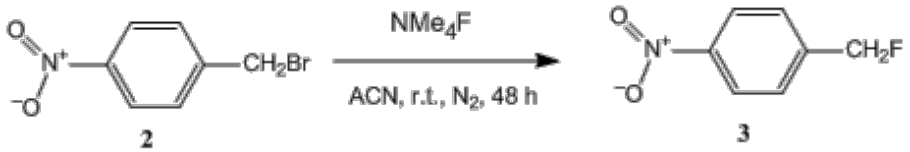
Substrates

1. 4-nitrotoluene (**1**), Aldrich, 99 %
2. 4-nitrobenzyl bromide (**2**), Aldrich, 99 %
3. 4-nitrobenzyl iodide (**4**), Aldrich, 99 %

Electrolytes

1. tetra-n-butylammonium tetrafluoroborate (NBu_4BF_4), Aldrich > 99%
2. tetra-n-methyl ammonium fluoride, Aldrich > 97%

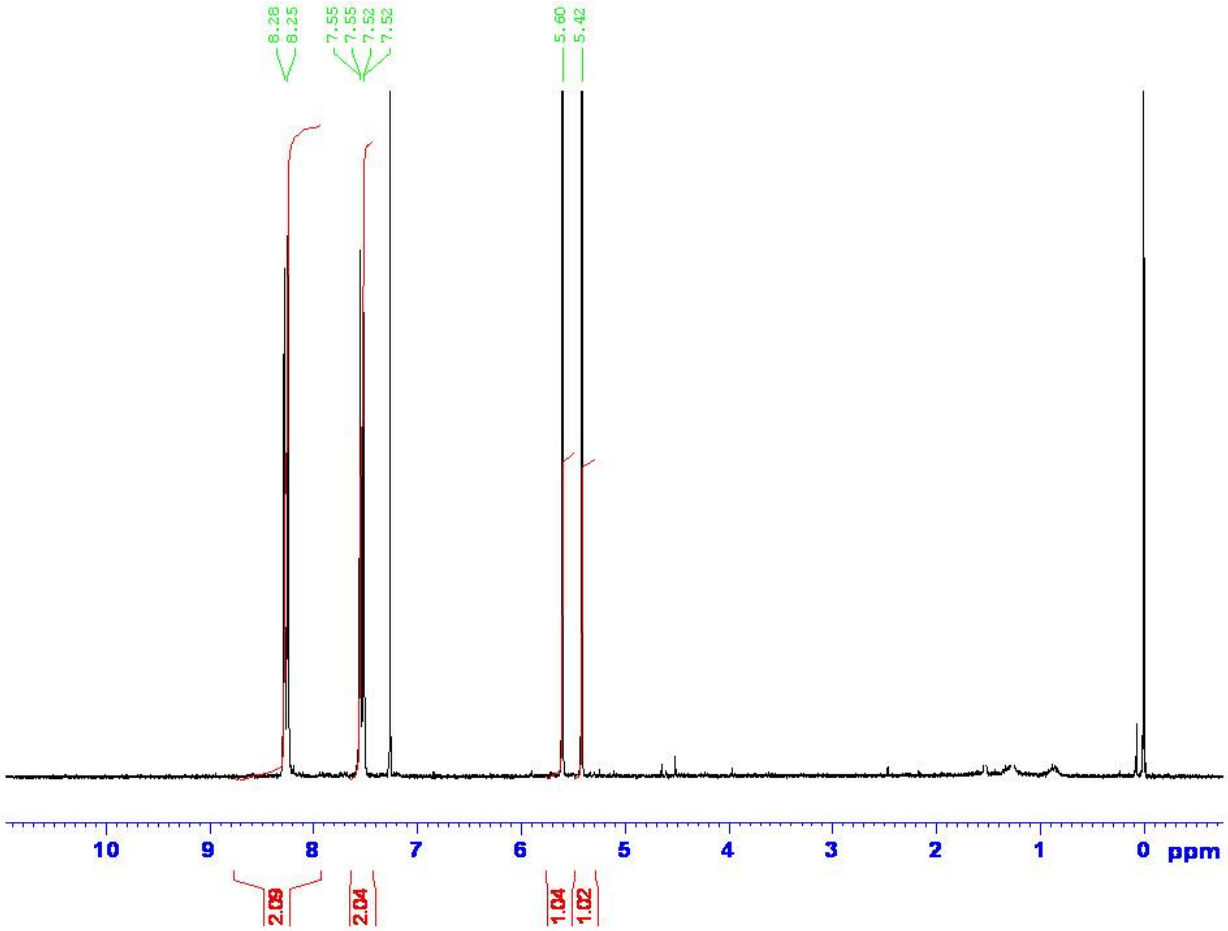
Synthesis of 4-nitrobenzyl fluoride (3).



2 **3**

90 %

Tetramethyl ammonium fluoride (0.1583 g, 1.70 mmol) was slowly added under nitrogen atmosphere to a solution of 4-nitrobenzyl bromide (**2**) (300mg, 1.38mmol) in 100 mL of dichloromethane (DCM) at room temperature. The reaction was stirred and monitor through Thin Layer Chromatography (TLC), after 6 hours, 0.260 g (2.8 mmol) of tetramethyl ammonium fluoride were added. This step of the reaction has a duration of 6 hours, and then we add tetra-n-methyl ammonium fluoride (0.2608g, 2.8 mmol). After 48 h, the reactant was fully consumed. The resulting mixture was extracted with water (3 × 100 mL). Organic phases dried with $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the resulting crude product was purified using column chromatography through silica (pentane/dichlorometane, 6:4) to afford 112 mg of the pure product as pale yellow solid.



1. ^{1}H NMR (250 MHz, CH_2Cl_2) of a) 4-nitrobenzyl fluoride δ: 8.27 (d, *J* = 8.19 Hz, *J* = 1.33 Hz 2H), 7.54 (d, *J* = 7.86 Hz, *J* = 1.18 Hz, 2H), 5.42 (s, 2H). b) 2 δ: 8.27 (d, *J* = 8.19 Hz, *J* = 1.33 Hz 2H), 7.54 (d, *J* = 7.86 Hz, *J* = 1.18 Hz, 2H), 5.42 (s, 2H)

The compound was characterized by comparison of pure samples using Nuclear Magnetic Resonance of Proton (^{1}H NMR, Figure 1), Gas Chromatography (GC) and Gas Chromatography-Mass Spectrometry (GC-MS).

Cyclic voltammetry experiments.

An electrochemical conical cell was used for the set-up of the three-electrode system. For cyclic voltammetry experiments, the working electrode was, in all cases, a glassy carbon disk of a diameter of 1.0 mm. It was polished using a 1 μm diamond paste. The counter electrode was a platimun disk of a diameter of 0.3 cm. All of the potentials are reported versus a Saturated Calomel Electrode (SCE) isolated from the working electrode compartment by a salt bridge. The salt solution of the reference calomel electrode is separated from the electrochemical solution

by a salt-bridge ended with a frit, which is made of a ceramic material, allowing ionic conduction between the two solutions and avoiding appreciable contamination.

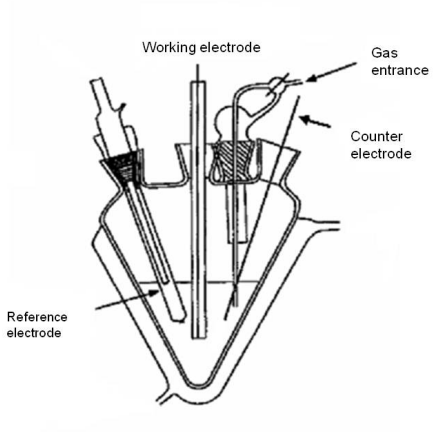


Figure 2. Electrochemical cell

Solutions were prepared using DMF as a solvent and they were purged with argon before the measurements, and N_2 was allowed to flow under the solution during the measurements. The concentration of the nitrobenzyl halides was ~10^{-3} M; while the supporting electrolyte concentration was 0.1 M of tetra n-butylammonium tetrafluoroborate.
Cyclic Voltammetry experiments with the electroactive species in DMF were performed at different scan rates starting from 0.1 Vs^{-1} to 1000 Vs^{-1}. Since, the ohmic drop may be one of the main sources of error at fast scan rates, it was electronically corrected (positive feedback) in the range 0.1-1000 Vs^{-1}.

Working electrode calibration

The first step was calibrating the working electrode. For such a purpose, we decided to use fluorenone, as a redox probe, since it is a well-known one electron reduction electroactive substance. Thus, we prepared several fluorenone solutions of different concentrations, those solutions contained tetra n-butylammonium tetrafluoroborate as supporting electrolyte (0.1 M). Solutions were prepared using DMF as a solvent and they were purged with argon before the measurements, and N_2 was allowed to flow under the solution during the measurements. The electron transfer shows a reversible wave at -1.28 V (E^o average) and the peak width 0.07 V (ΔEp average). Using this electrochemical set up the average value for the current function is 3.1 $\mu A/mM(V\ s^{-1})^{1/2}$.

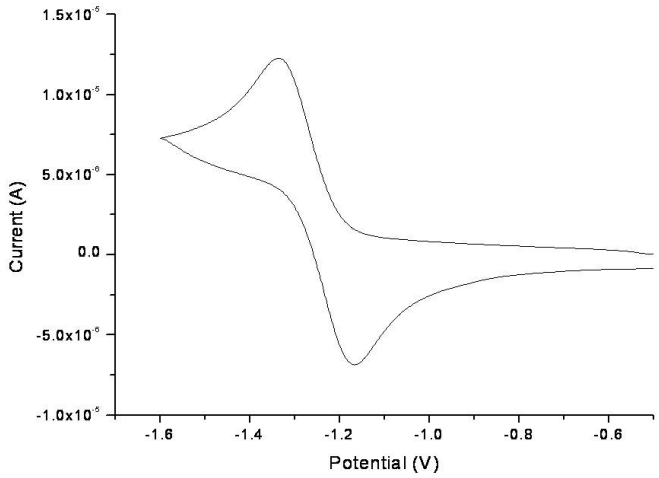


Figure 3. Cyclic Voltammetry of **fluorenone** (5.00 mM) in dimethylformanide (DMF) + 0.1M NBu_4BF_4 at room temperature under N_2. Working electrode: Glassy Carbon disk electrode (0.1 mm diameter), Counter electrode: Platinium disk electrode (0.3 cm diameter), Reference electrode SCE. Scan rate 0.5 $V.s^{-1}$. Scan Range: -0.50/-1.60/-0.50 V.

Controlled potential electrolysis

General procedure for the electrosynthesis of nitrobenzyl halides: a solution of nitroaromatic compound (10 mM) in 10 mL of DMF, containing 0.3292 g of NBu_4BF_4 (0.1M) as supporting electrolyte, was prepared in a nitrogen atmosphere. Reductive controlled-potential electrolysis at different potentials vs SCE was performed using a carbon graphite rod as a working electrode. After the passage of the desired number of Faradays, the electrolysis was stopped. The resulting mixture was extracted with toluene (3 x 10 mL). Organic phases were combined, dried (Na_2SO_4) and filtered. The solvent was evaporated under reduced pressure and the resulting crude product was analyzed by cyclic voltammetry (CV), gas chromatography (GC), gas chromatography-mass spectrometry (GC-MS) and ^1H RMN. The chemical features of the resulting products were finally checked with pure samples of the same products.

Instrumentation

Cyclic voltammetry and electrolysis

Cyclic voltammetry at low scan rates and electrosynthesis experiments were carried out in the same cell and using a PAR 273A potentiostat.

Cyclic voltammetry at moderate scan rates was performed using an apparatus composed of a homemade solid-state amplifier potentiostat with positive feedback iR drop compensation and a

Tacussel GSTP 4 generator. The voltammograms were displayed on a Tektronix (2212) instrument.

Gas Chromatography (GC)

A PerkinElmer Clarus 500 Gas Chromatograph, which is a fully automated gas chromatograph, was used for performing a large numbers of routine analyses. All instrument functions are set up and monitored through either a touch screen or a personal computer.

Gas Chromatography-Mass Spectrometry (GC-MS)

An Agilent Technologies 7890 A GC system coupled to a mass detector from the Organic Chemistry Unit of the UAB was used for analyzing the electrolyzed samples and pure compounds.

Nuclear Magnetic Resonance

^{1}H NMR spectra were performed using a Bruker DPX250 (250MHz) instrument available from the NMR Services of the UAB.

Results and discussion

The objective of this section is to disclose the electrochemical reduction mechanism of 4-nitrobenzyl fluoride and iodide. To fulfill this ambitious goal, before to start with electrochemical studies of the above-mentioned compounds, it is mandatory to broach two previous points. First, to study the cathodic electrochemical behavior of the 4 nitrotoluene so as to be familiar with the electrochemical features of nitroaromatic compounds. Second, to revise the electrochemical result the electrochemical reduction mechanism of 4-nitrobenzyl bromide so as to learn about the reactivity of the anion radical formed. In both cases, these previous electrochemical studies will allow not only to know and manage the electrochemical techniques but also to optimize the chemical strategies that will be used to reach our final goals.

Electrochemical behavior of 4-nitrotoluene (1)

4-nitrotluene (**1**) was selected as reduction probe to conduct our electrochemical experiments. This compound shows two reduction waves in a cathodic scan. The first electron transfer of this compound corresponds to one electron-reversible electron transfer cathodic peak potential (Epc) at -1.25 V vs. Saturated Calomel Electrode (SCE) at 0.5 Vs^{-1} which leads to its corresponding anion radical (Figure 1a). The results depicted in Table 1 indicate that there is no dependence of the standard potential (E°), values with the scan rate and concentration. Moreover, the fact that the first reduction wave is reversible as well as the ΔEp value is close to 75 mV indicates that this first electron transfer is a fast process.

The second wave with Epc of -2.24 V vs. SCE is a chemically irreversible multi-electron transfer (Figure 1b) where the reduction of the nitroso group takes place. It is possible to detect the formation of the nitroso derivative after the second electron transfer; an oxidation wave appears at Epa -0.90 V vs. SCE in the anodic counter scan. This oxidation wave corresponds to the oxidation of the nitroso anion radical to its neutral derivative after the second reduction (Scheme 1).

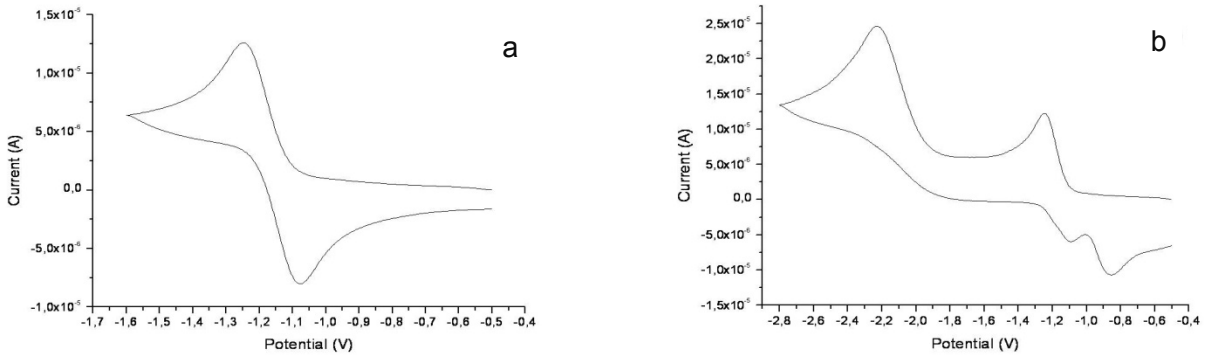
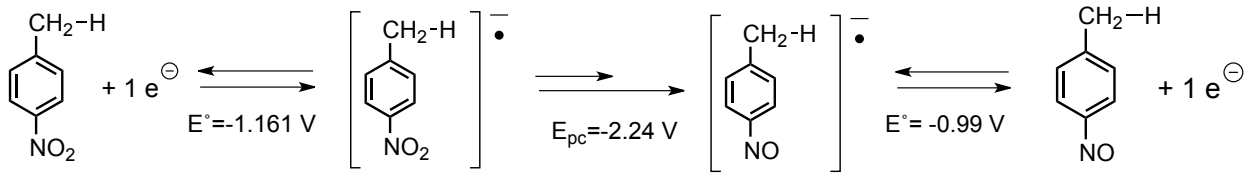


Figure 1. Cyclic Voltammetry of 1 (5.00 mM) in dimethylformanide (DMF) + 0.1M NBu_4BF_4 at room temperature under N_2. Working electrode: Glassy Carbon disk electrode (0.1 mm diameter), Counter electrode: platinium disk electrode (0.3 cm diameter), Reference electrode SCE, Scan rate 0.5 $V.s^{-1}$. a) Scan Range: -0.50/-1.60/-0.50 V vs. SCE b) Scan Range -0.5/-2.8/-0.5 V vs. SCE



1

Scheme 1

Table 1. Electrochemical features of the first electron transfer of compound 1

Scan rate (Vs^{-1})	Epc (V)	E^0 (V)	Peak width (V)	Ipc/cv½ ($\mu A/mM(V\ s^{-1})^{1/2}$)
0.05	-1.21	-1.164	0.06	3.8
0.1	-1.21	-1.159	0.06	3.7
0.3	-1.23	-1.162	0.07	3.5
0.5	-1.25	-1.161	0.08	3.3
0.7	-1.26	-1.163	0.08	3.1
1.0	-1.28	-1.160	0.09	2.9
Average		-1.161	0.07	3.4
Standard deviation		0.001	0.01	0.3

Electrochemical behavior of 4-nitrobenzyl bromide (2)

A typical cyclic voltammogram is given in Figure 2a. The cyclic voltammetry behavior of 4-nitrobenzyl bromide (2), at low scan rates in DMF using NBu_4BF_4 (0.1 M) as supporting

electrolyte, shows a first irreversible reduction wave at -0.83 V vs. SCE (Figure 2a, Inset). If the corresponding anodic counter scan is recorded up to 1.4 V, it is possible to distinguish the oxidation wave at + 0.85 V vs. SCE is also detected (Figure 2a). Finally, it is possible to differentiate a second reduction reversible wave at -1.23 V vs. SCE (figure 2b). Previously studies made at scan rate of 1225 Vs^{-1}, shows one electron reversible wave corresponding to the formation of the radical anion (E^0=-1.15 V vs. SCE)[19]. Based in that information, the anodic peak at 0.85 V as well as the cathodic peak at -1.23 V must be related with the products formed after this first electron transfer. The number of electrons involve in the first reduction process is determined by comparison with the fluorenone, our standard, in the same medium and with the same electrochemical set-up. The overall process is consistent with a one-electron reduction wave (Table 2)

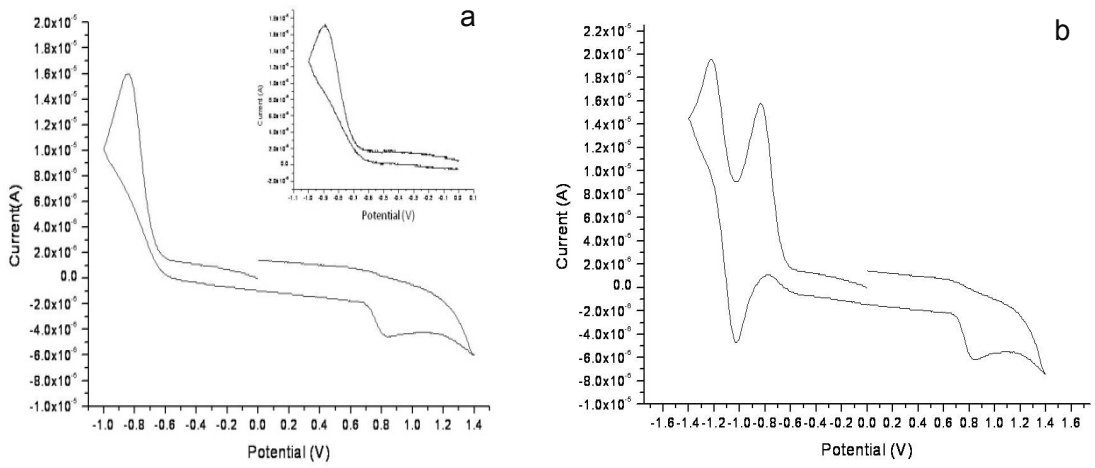


Figure 2. Cyclic Voltammetry of 2 (5 mM) in DMF + 0.1M NBu_4BF_4at room temperature under N_2 atmosphere at room temperature. Working electrode glassy carbon electrode (0.1mm diameter). Counter electrode platinum disk electrode 0.3 cm diameter. Reference electrode SCE. Scan Rate 0.5 V s^{-1}. a) 0.0/-1.0/1.4/0.0 V (Insert scan range: 0.0/-1.0/0.0 V) b) Scan Range: 0.0/-1.40/1.40/0.0 V.

The irreversibility of this first electron transfer would presumably lead to the nitrobenzyl radical and the bromide anion. The oxidation wave at +0.85 V vs SCE can be assigned to the electrochemical response of the bromide anion formed after the first reduction process since a pure solution of potassium bromide is analyzed in terms of cyclic voltammetry, the presence of an oxidation peak is revealed at +0.85 V under the same experimental conditions (Figure 3).

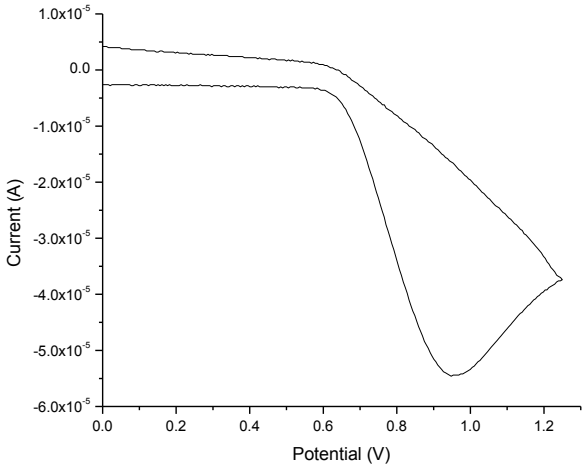


Figure 3. Cyclic Voltammogram of 5 mM potassium bromide in dimethylformanide (DMF) + 0.1M NBu_4BF_4 at room temperature under N_2. Working electrode: Glassy Carbon disk electrode (0.1 mm diameter), Counter electrode: Platinium disk electrode (0.3 cm diameter), Reference electrode SCE, Scan rate, v = 0.5 V s^{-1}.

The cyclic voltammogram of a commercial sample of 4,4'-dinitrobibenzyl exhibits a two electron reversible wave at the same potential as the product formed after the first reduction wave of **2** at -1.17 V (figure 4). Hence, the appearance of a second reduction wave after the first reduction process should be attributed to the two-electron reduction of the 4,4'-dinitrobibenzyl.

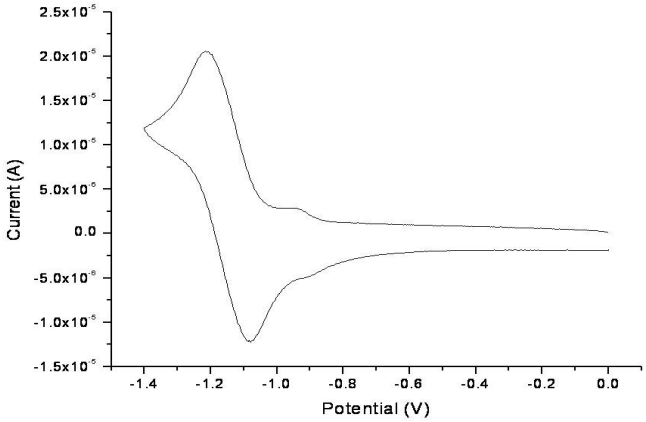
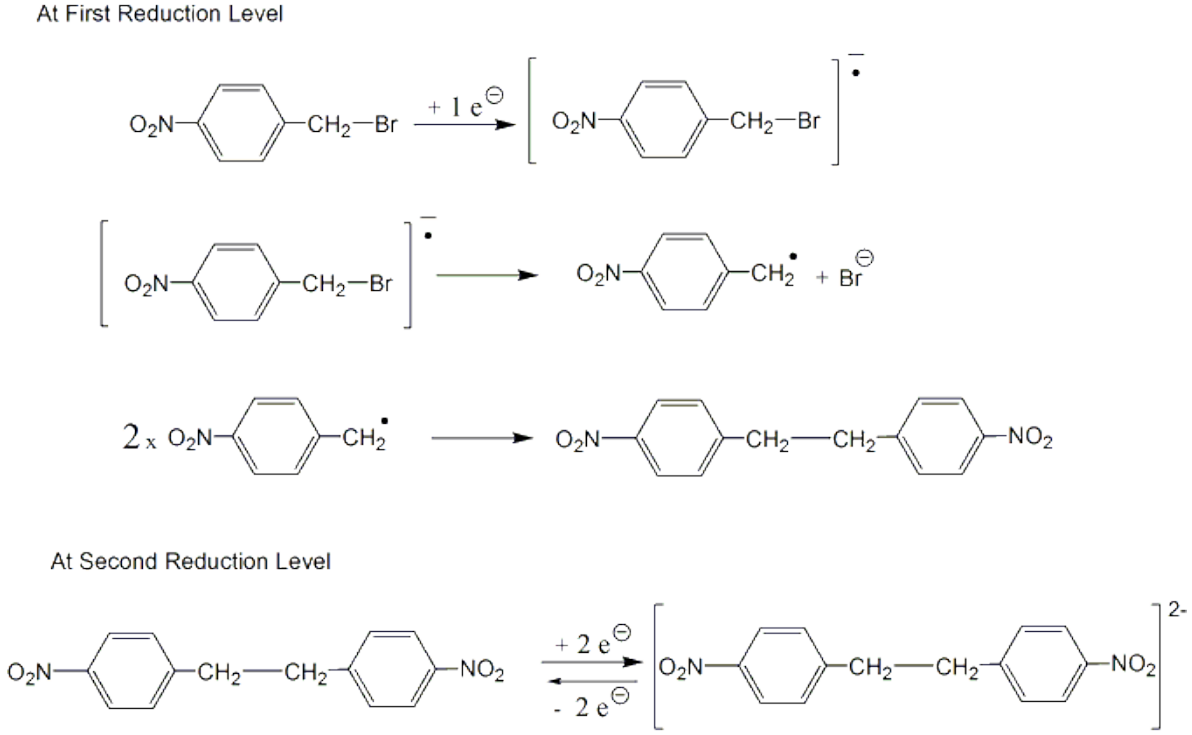


Figure 4. Cyclic Voltammogram of 4,4-dinitrodibenzyl in dimethylformanide (DMF) + 0.1M NBu_4BF_4 at room temperature under N_2. Working electrode: Glassy Carbon disk electrode (0.1 mm diameter), Counter electrode: Platinium disk electrode (0.3 cm diameter), Reference electrode SCE, Scan rate, v = 0.5 V s^{-1}.

These results confirm previous studies performed in our research group[19] revealed that the electrochemical reduction of the 4-nitrobenzyl bromide at -1.00 V at after the passage of 1F

yields quantitatively to the 4,4'-dinitrobibenzyl through supports an EC mechanism. This mechanism supports a radical coupling reaction, which requires that the 4-nitrobenzyl radical must be reduced at more negative potentials than -1.10 V (Scheme 2).



Scheme 2

Table 2. Electrochemical features of the first electron transfer of compound 2

Scan rate (V s^{-1})	Epc (V)	Peak width (V)	Ipc/cv½ (μA/mM(V s^{-1})$^{1/2}$)
0.05	-0.81	0.10	3.5
0.1	-0.82	0.10	3.6
0.3	-0.85	0.09	3.4
0.5	-0.89	0.09	3.7
0.7	-0.93	0.12	3.3
1	-0.94	0.15	3.0
Average		0.11	3.4
Standard deviation		0.02	0.2

The measured parameters of an electrode process depend on the extent to which that reaction proceeds during the course of the electrochemical experiment. Potential step and

voltammetric methods are applicable to reactions that are fast enough to occur within the diffusion layer near the electrode surface. The directions and extents of variation of these provide diagnostic criteria for establishing the type of mechanism involved, and the measurements themselves provide data for evaluation of the magnitudes of the rate constants of the coupled reactions.

We proceed to calculate the alpha value for the first electron transfer of the 4-nitrobenzyl bromide. We calculate the alpha value compare the Epc with the log of the scan rate, the slope of this plot is $\left(\frac{\partial Epc}{\partial \log v}\right) = \frac{-0.0296}{\alpha}$. The value we obtained by this method is 0.29, this value confirm the fact about the slow electron transfer.

The slope for $\left(\frac{\partial Epc}{\partial \log c}\right)$ is closed to 0, which indicates that the reaction linked to the electron transfer is a first order reaction.

Electrochemical behavior of 4-nitrobenzyl iodide (3)

Similar electrochemical behavior to the above-mentioned for 4-nitrobenzyl bromide is observed for the other 4-nitrobenzyl iodide. A first one-electron reduction irreversible wave at -0.93 V vs. SCE (Figure 5a), which presumably will lead to nitrobenzyl radical and iodide. Figure 5b shows that at longer scan range, a second one-electron reversible wave is found at E° = -1.17 V as well as two oxidation peaks at 0.65 V and 0.97 V vs. SCE at the corresponding anodic scan.

The study by cyclic voltammetry at different scan rate permits to establish the thermodynamics and the kinetic values associate to the first electron transfer for 3 (Table 3). From those assays it is possible to calculate the order of the reaction linked to the electron transfer and electron transfer coefficient, which is calculated using the following equation $\left(\frac{\partial Epc}{\partial \log v}\right) = \frac{-0.0296}{\alpha}$ for this case alpha value is 0.28 that is representative of a slow electron transfer. Since there is not dependence of the Epc vs. log v, it can be concluded that the chemical reaction linked to the electron transfer is a first order reaction.

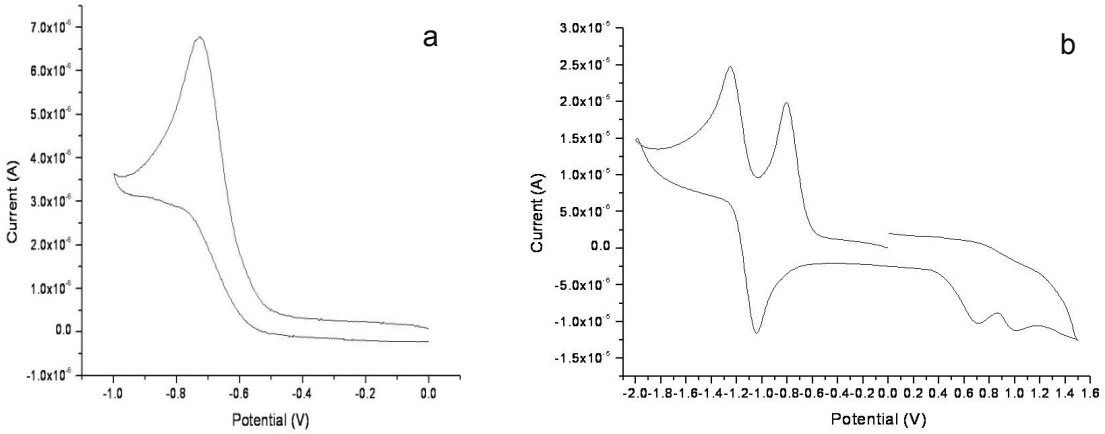
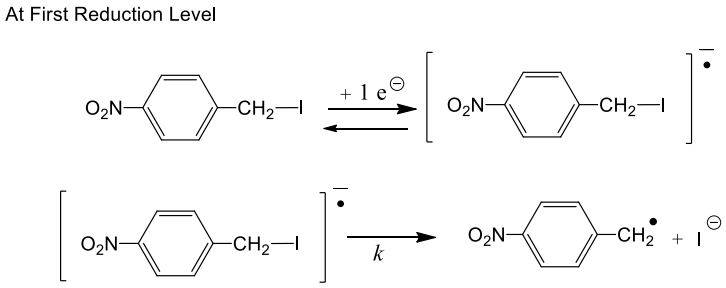


Figure 5. Cyclic Voltammetry of 3 5 mM in DMF + 0.1 M of NBu_4BF_4 at room temperature under N_2 atmosphere. Scan rate 0.5 Vs^{-1} Working electrode glassy carbon electrode 0.1mm diamter. Counter electrode platinum disk 0.3 cm diameter. Reference electrode SCE. a)Scan range 0.0/-1.1/0.0 V b) scan range 0.0/-2.0/1.5/0.0 V

Hence an EC mechanism is operating in this case (Scheme 3).



Scheme 3

Table 3. Electrochemical features of the first electron transfer of compound 3

Scan rate (Vs^{-1})	Epc (V)	Peak width (V)	Ipc/cv½ (μA/mM($V\ s^{-1}$)$^{1/2}$)
0.05	-0.72	0.07	3.9
0.1	-0.73	0.08	2.9
0.3	-0.77	0.08	3.3
0.5	-0.81	0.10	3.5
0.7	-0.83	0.10	3.3
1	-0.85	0.11	3.3
Average		0.09	3.4
Standard deviation		0.01	0.3

The electrochemical features of iodide anion are determined by the cyclic voltammetry. Figure 6 shows a typical cyclic voltammogram of a 5 mM potassium iodide solution in DMF, which contains 0.1M NBu_4BF_4. The comparison between Figure 5b and 6 shows noticeable similarities, both voltammograms shows oxidation peaks at reductions Epa of 0.65 V and 0.90 V vs. SCE. The first oxidation peak is assigned to the oxidation of iodide, whereas according to the literature the second anodic peak is related with the oxidation of I_3^-. [20] For both compounds these electron transfers are irreversible.

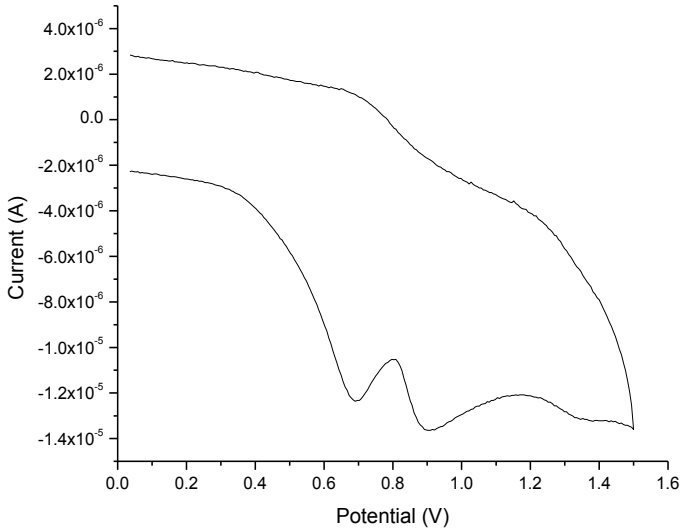


Figure 6. Cyclic Voltammetry of potassium iodide 5 mM in DMF + 0.1 M of NBu_4BF_4 at room temperature under N_2 atmosphere. Scan rate 0.5 Vs^{-1} Working electrode glassy carbon electrode 0.1mm diamter. Counter electrode platinum disk 0.3 cm diameter. Reference electrode SCE. a)Scan range 0.0/-1.5/1.5/0.0V

In order to characterize the electroactive products obtained after this first electron transfer, controlled-potential electrolysis were performed at -1.0 V and -1.5 V vs. SCE, after the passage of 1F and 2F, respectively, the electrochemical reactions were followed using cyclic voltammetry.

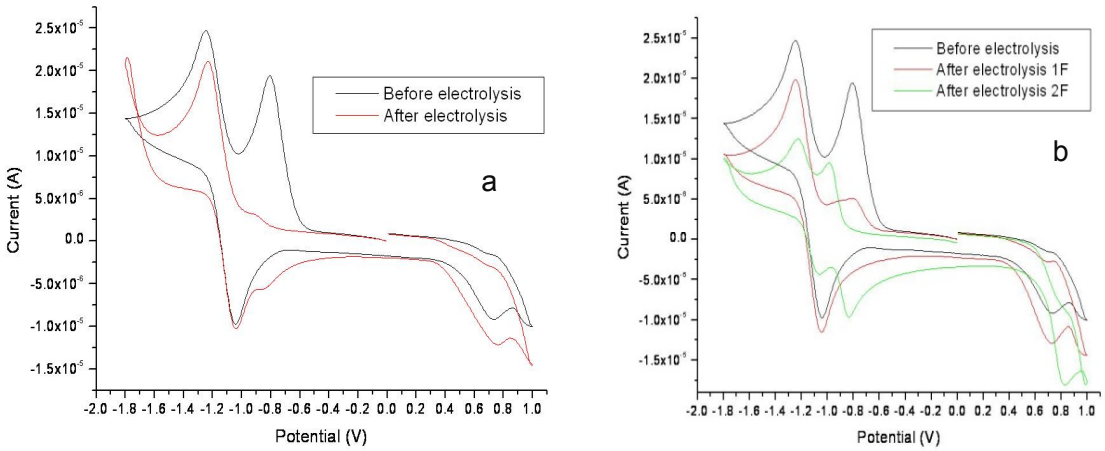
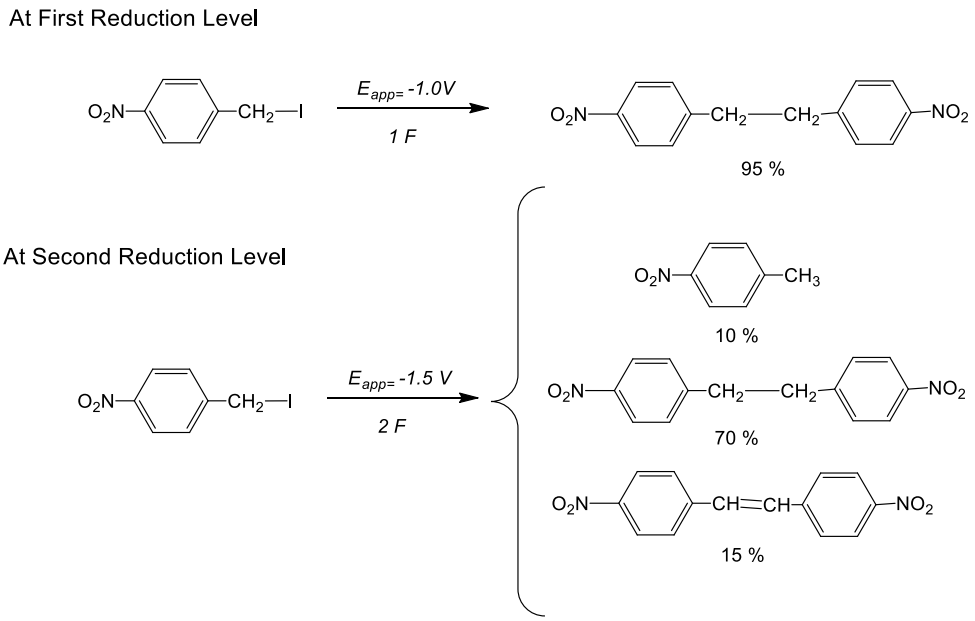


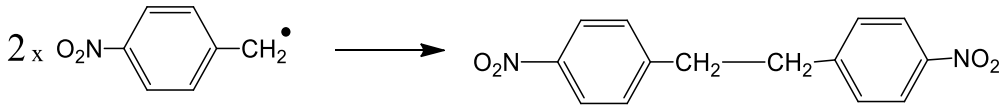
Figure 7 Cyclic Voltammetry of 3 5 mM in DMF + 0.1 M of NBu_4BF_4 at room temperature under N_2 atmosphere. Scan rate 0.5 V s^{-1} Working electrode glassy carbon electrode 0.1mm diameter. Counter electrode platinum disk 0.3cm diameter. Reference electrode SCE. a) electrolysis at -1.0 V Scan range 0.0/-1.8/1.0/0.0V b) electrolysis at -1.5 V Scan range 0.0/-1.8/1.0/0.0V

Figure 7a shows the decrease of the first reduction as well as the growing of the second reduction and oxidation peaks, respectively, after the passage of 1F at -1.0 V. A similar study is performed (Figure 9b), after the passage of 1F and 2F at -1.5 V is seems that a new reduction product is obtained (reduction peak at -0.80 V). The electrolyzed solutions were analyzed by 1H RMN, GC and GC-MS (Scheme 4).



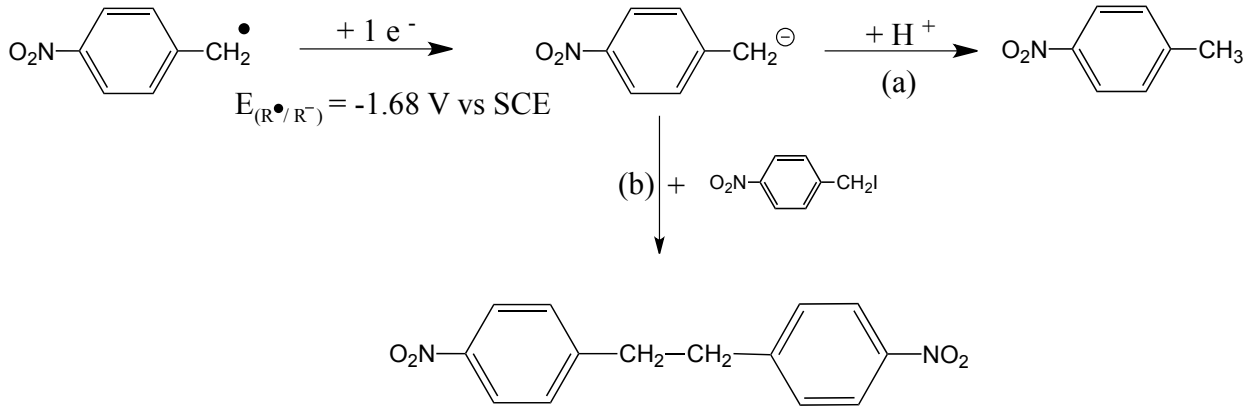
Scheme 4

It is important to remark that after electrolysis of 4-nitrobenzyl iodide solutions at each of the above-mentioned potentials, -1.0 V and -1.5 V, there are different distribution products. When the electrolysis is performed at -1.0 V after the passage of 1F, the only product obtained is the 4,4'-dinitrobibenzyl, so there is the chemical reaction linked to this first electron transfer is a radical-radical coupling (Scheme 5)



Scheme 5

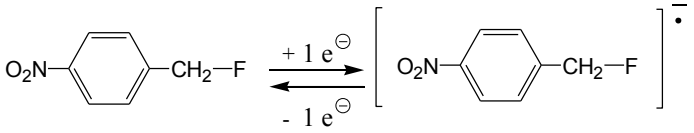
When the potential applied is -1.5 V after the passage of 2F, there is a remarkable change in the distribution products, the main product obtained is still the 4,4'-dinitrobibenzyl but there are important amounts of 4-nitrotoluene and 4,4'-trans-dintirostilbene. The formation of 4 nitrotoluene is perfectly justifiable in terms of the radical reduction potential value is closed to the potential applied in the electrolysis process. The presence of 4,4-trans-dinitrostilbene should be related either with the reduction of the 4,4'-dinibibenzyl or 4-nitrotoluene in those reaction conditions. Those, at this point it is able to conclude that the 4-nitrobenzyl radical anion breaks very fast and radical is formed so close to the electrode surface that the reduction of the radical is able to outrun the radical-radical dimerisation. Later, the 4 nitrobenzyl anion will either act as a base (minor reaction, Scheme 6 path a) affording the 4-nitrotoluene compound (15 %) or a nucleophile (major reaction, Scheme 6 path b) leading to the corresponding dimer (70 %). It is known[19] that the reduction potential value of the redox couple p-nitrobenzyl radical/p-nitrobenzyl anion ($E(R^{\bullet}/R^{-})$) is - 1.68V vs SCE , thus the radical could be reduce at this potential value.



Scheme 6

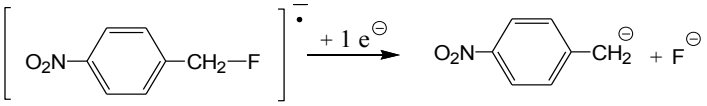
Electrochemical behavior of 4-nitrobenzyl fluoride (4)

The 4-nitrobenzyl fluoride (4) has also been investigated by means of cyclic voltammetry in DMF + 0.1 M Bu_4NBF_4. Figure 8a shows the typical cyclic voltammogram of this compound at low scan rate. The first wave corresponds to the reversible reduction of the substrate and the standard potential of this compound is summarized in Table 5. Hence, **4** take reversibly a first electron, which is mainly located on the nitro group according to the value of the standard potential (about –1.016 V vs. SCE) to form an anion radical (Scheme 7)



Scheme 7

A second irreversible one electron reduction wave and a third irreversible multielectronic wave appear at -1.80 V, whereas an oxidation wave corresponding to the nitroso derivatives appears at -2.40 V (Figure 8b). Focusing on the first two reduction waves, since the obtention of nitroso derivates is not the main interest in this study, it fairly to think that the anion radical takes a second electron and the dianion would react, it may break at the level of carbon-fluorine bond (Scheme 8).



Scheme 8

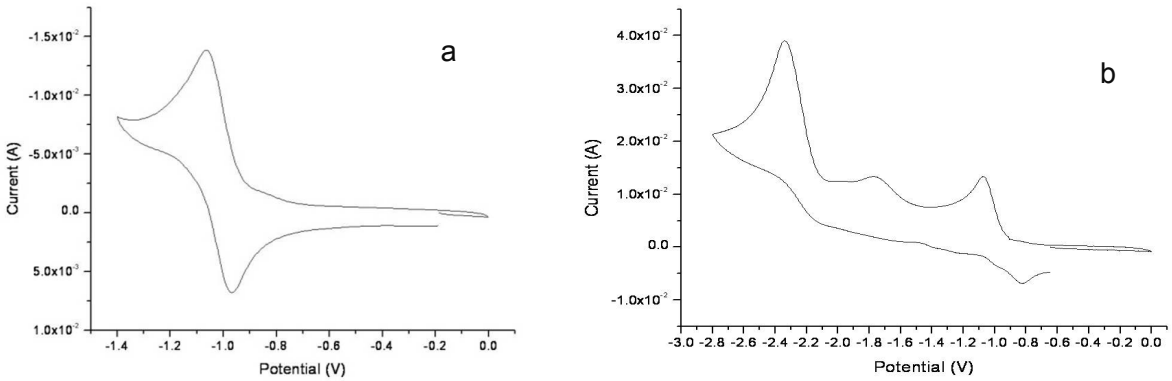


Figure 8. Cyclic Voltammetry of 4 (5 mM) in DMF + 0.1M NBu_4BF_4 at room temperature under N_2 atmosphere. Working electrode glassy carbon electrode (0.1mm diamter). Counter electrode platinum disk electrode 10.3 cm

diameter. Reference electrode SCE. Scan Rate 0.5 V s^{-1}. a) scan Range: 0.0/-1.40/0.0 V,b) Scan Range: 0.0/-2.80/0.0 V.

Table 4: Electrochemical Features of 5mM 4-nitrobenzyl Fluoride

Scan Rate (Vs^{-1})	Epc (V)		Peak width (V)		Ipc/cv½ ($\mu A/mM(V\ s^{-1})^{1/2}$)	E^0 (V)
	1rst wave	2nd wave	1rst wave	2nd wave	1rst wave	1rst wave
0.05	-1.05	-1.76	0.07	0.058	3.87	-1.013
0.1	-1.05	-1.67	0.07	0.049	3.6	-1.013
0.3	-1.06	-1.68	0.07	0.059	3.5	-1.012
0.5	-1.06	-1.71	0.07	0.062	3.4	-1.017
0.7	-1.06	-1.72	0.07	0.065	3.3	-1.015
1	-1.06	-1.72	0.07	0.070	3.3	-1.016
10	-1.10	-1.86	0.11	0.072	3.3	-1.025
20	-1.12	-1.95	0.11	0.112	3.0	-1.014
5	-1.08	-1.80	0.08	0.071	3.1	-1.018
Average					3.4	-1.016
Standard deviation					0.2	0.003

These results are confirmed by controlled potential electrolysis. Electrolysis was carried out at -0.9 V, -1.1 V, -1.4 V and -2-2 V, those potential are slightly more negative than the first and second peak potential, after the passage of 1F or 2F. The electrolyzed solutions are analyzed in term of cyclic voltammetry, gas phase chromatography and gas chromatography coupled with mass spectrometry.

When the electrolysis is performed at low reduction potential values -0.9 V vs. SCE, just at the beginning of the first reduction wave, the current flow at this potential is not enough to electrolyse the sample. Therefore, the starting material (4) is fully recovered at the end of the process after the passage of 1F. (Scheme 9)

Scheme 9

Surprisingly, when the potential applied is -1.1 V or -1.4 V before the second reduction wave, the monitor of the reaction (Figure 9a) as well as the analysis of the products at the end of the electrolysis, after the passage of 1F reveals the formation of 4,4'-dinitrobibenzyl and 4,4'-cis-dinitrostilbene (Scheme 10). The amount of 4,4'-cis-dinistrostilbene is higher when the potential value goes from -1.1 V to -1.4 V. These results seem to indicate that there is either a slow chemical reaction linked to the electron transfer (scheme 11 path a), or a radical anion dimerization reaction (Scheme 11 path b)

Moreover, the yield of 4,4'-cis-dinitrostilbene, which has not been obtained in the electrochemical reduction of either the bromine or iodide derivates after the first reduction wave, indicates that the fluorine anion would react with the 4,4'-dinitrobibenzyl leading to the corresponding stilbene derivate.

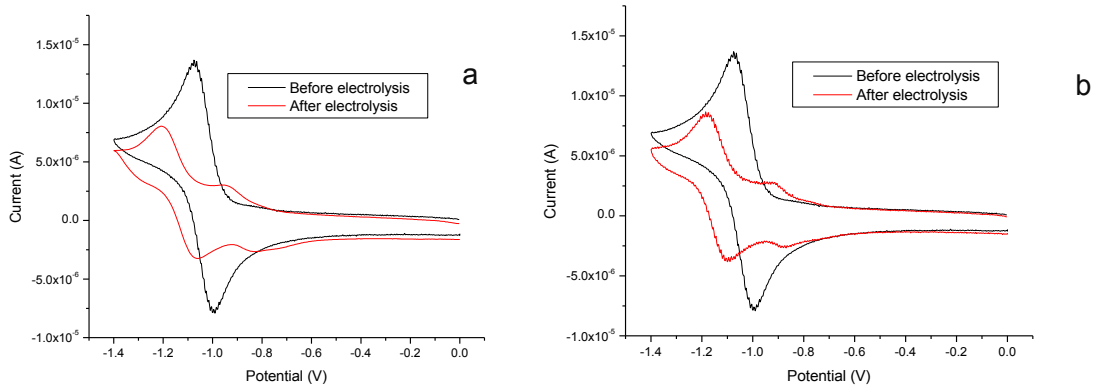
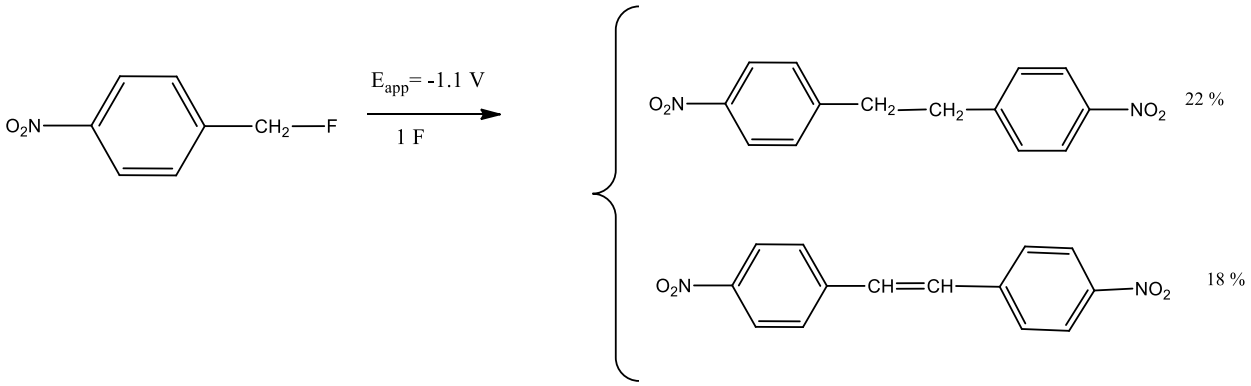
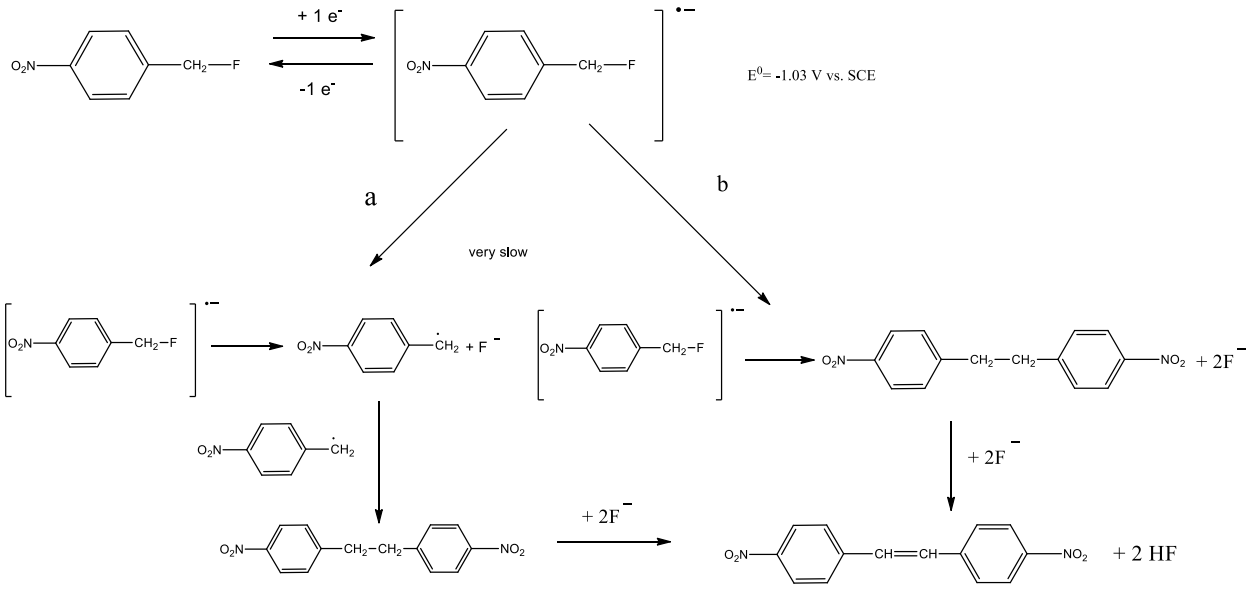


Figure 9 Cyclic Voltammetry of 4 (5 mM) in DMF + 0.1M NBu_4BF_4 at room temperature under N_2 atmosphere. Working electrode glassy carbon electrode (0.1mm diamter). Counter electrode platinum disk electrode 0.3 cm diameter. Reference electrode SCE. Scan Rate 0.5 V s^{-1}. a) electrolysis at -1.4 V scan range: 0.0/-1.40/0.0 V,b) electrolysis at -2.2 V scan range: 0.0/-1.40/0.0 V.

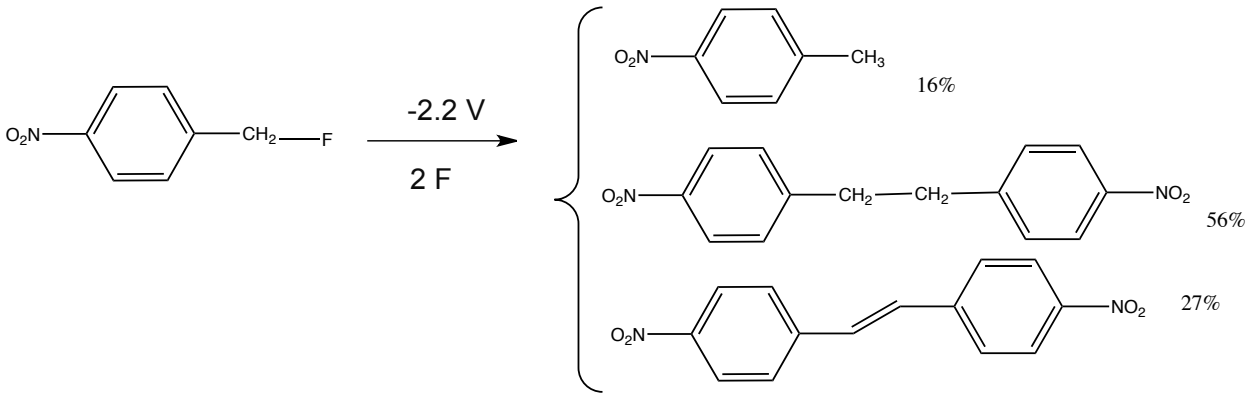


Scheme 10

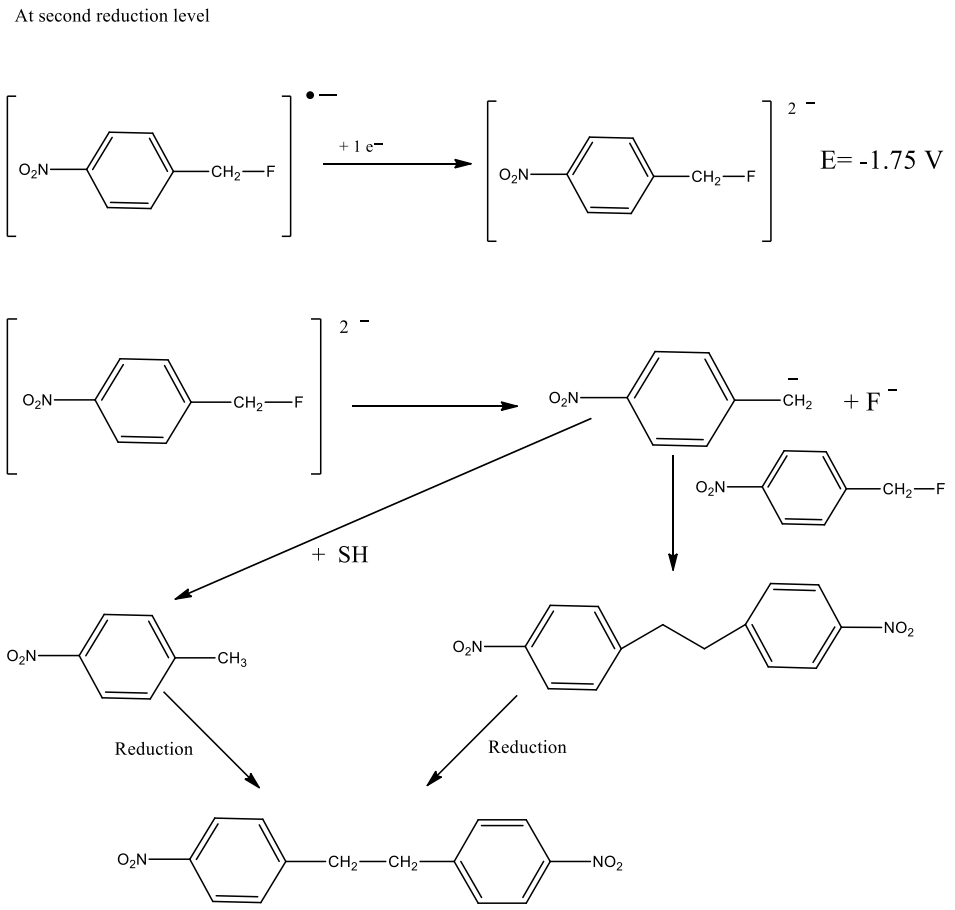


Scheme 11

When, electrolysis is performed until 2F at a potential slightly more negative than the second peak potential, -2.2 V, similar products are obtained (Figure 9b). However, a closer look to the nature of the reaction products reveals important mechanistic differences (Scheme 12). The formation of 4-nitrotoluene should be related to the formation of the 4-nitrobenzyl anion. This means that the 4-nitrobenzyl fluoride dianion has a faster cleavage that the corresponding anion radical. This dianion can either react with a molecule of **4** following a S_N2 reaction leading to 4,4'-dinitrobibenzyl or being protonated in the reaction media yielding the 4-nitrotoluene (1). Since, both products are electroactive at this potential the formation of the 4,4'-trans-dinitrostilbene could be related to the reduction of 4-nitrotoluene or 4,4'-dintitrobibenzyl (Scheme 13).

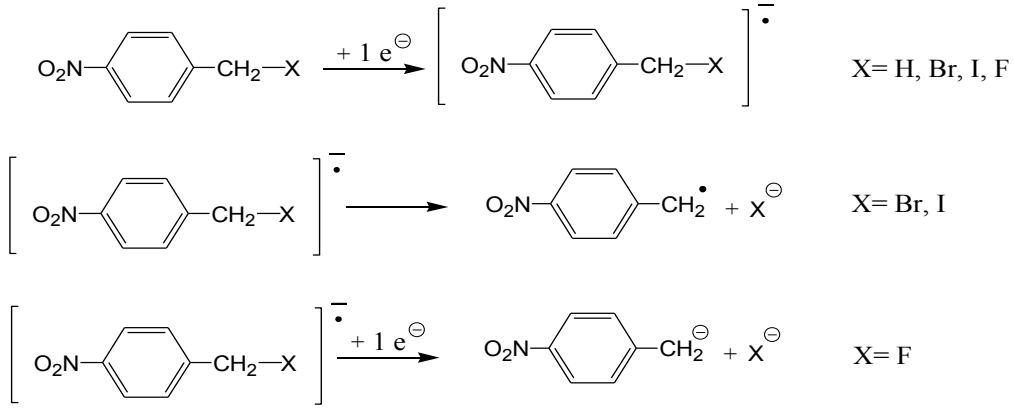


Scheme 12



Scheme 13

Thermodynamics

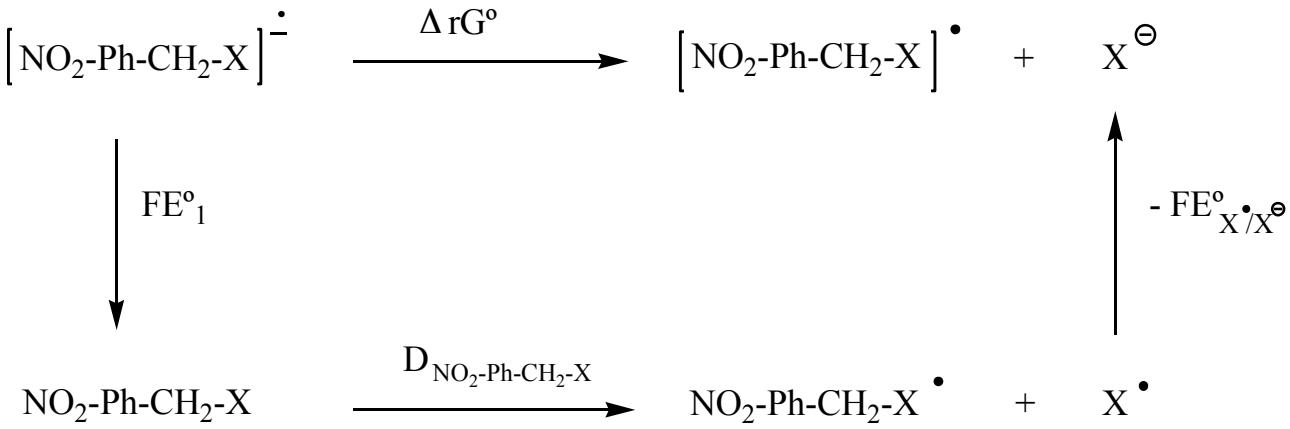


Scheme 14

We have just demonstrated that the C-Br and C-I bond cleavage for the compounds **2** and **3** appears through the mechanism described in scheme 14. However, compounds **1** (C-H)

and **4** (C-F) do not undergo through dissociative electron transfer reaction at the first electron transfer level and in the cyclic voltammetry time scale. However, compound **4** shows a C-F bond cleavage at the second electron transfer level.

The observed reactivity can be related to the ability of the aromatic radical anions to undergo cleavage of the carbon halogen bond. The order H<F<Cl<Br<I is the same as reported in the literature for other nitro and cyano derivatives with the peculiarity that in our case there is an stable "fluoride radical anion". Saveant et al. provided the theoretical background to analyze the relative fragmentation reactivity of the radical anions. Thus, leaving apart entropy effects (that must be very similar in all the cases and should be around 27.8 J/mol according to previous works published in the literature[21]), in this model the fragmentative reactivity is a function of the bond dissociation energy of the neutral substrate ($D_{NO2\text{-}Ph\text{-}CH2\text{-}X}$), the standard redox potential of the pair substrate:radical anion ($E_1°_{NO2\text{-}Ph\text{-}CH2\text{-}X}{}^{\text{anion radical}}{}_{/\,NO2\text{-}Ph\text{-}CH2\text{-}X}$) and the standard redox potential of the pair radical leaving group anion ($E°_X{}^{\text{radical}}{}_{/\,X}{}^{\text{anion}}$) (Scheme 15, Equation 1).



Scheme 15

Equation 1 $\Delta_r G^0 = D_{NO_2PhCH_2X} - T\Delta_r S^0 + F(E_1^0 - E^0_{X^\cdot/X^-})$

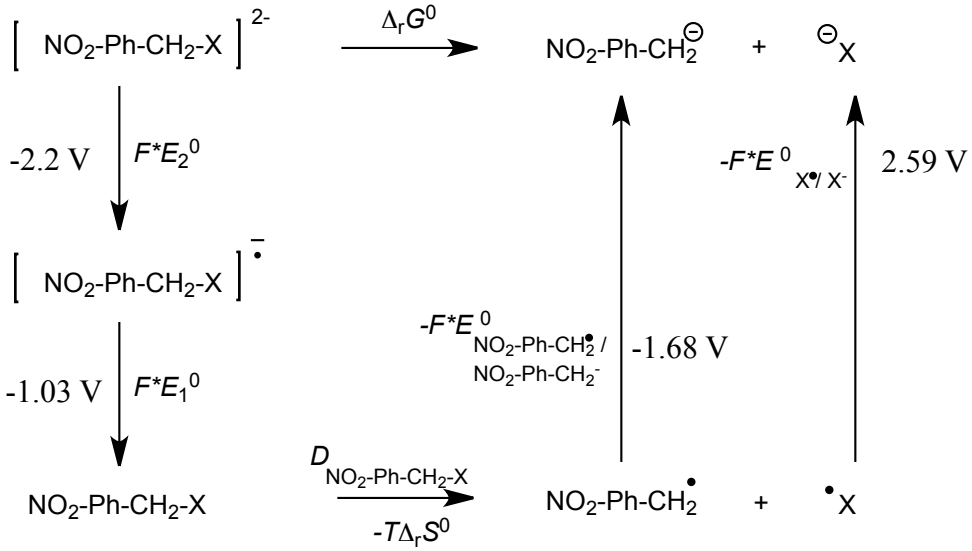
Taking into account the data depicted in Table 5 where it can be seen that ($E°_X{}^{\text{radical}}{}_{/\,X}{}^{\text{anion}}$) is a quite large value for all the halogenated compounds, it becomes clear that the bond dissociation energy ($D_{NO2\text{-}Ph\text{-}CH2\text{-}X}$) is the dominant factor. For the two compounds **2** and **3**, the standard free energy $\Delta_r G^0$ is negative; so, the reaction is thermodynamically favorable. Hence, in the case of compounds **1** and **4** higher reduction potential values are needed to break the CH_2-H or CH_2-F bonds, respectively. The observations made during the examination of the **4** indicate that this compound form a dimer instead of fallow a homolitic cleavage.

Table 5. Thermodynamic Data of 4-nitrobenzyl halides

Compound	$D_{NO2\text{-}Ph\text{-}CH2\text{-}X}$ (kJ·mol^{-1})	$T\Delta_rS^o$(J·mol^{-1})	$E^o_{X^{\cdot}/X^-}$(V)	E^o_1(V)	Δ_rG^o(kJ·mol^{-1})
		First Electron Transfer Level			
1 (X=H)	375	27.8	-0.84	- 1.17	+343.1
2 (X=Br)[a]	226	27.8	1.48	- 1.15	**-27.8**
3 (X=I)	180	27.8	0.99	- 1.13	**- 25.6**
4(X=F)	392	27.8	2.59	- 1.02	+15.8
X=Cl[a]	283	27.8	1.85	-1.13	**-5.57**

[a]Data from previous work performed in our research group.

It is important to note that in the case of compound **4** there is a second electron wave, which leads to dissociative electron transfer. According to previous results, the standard free energy Δ_rG^0 of the process should be a negative value. The design of a new thermodynamic cycle, which is presented in scheme 16, as well as the use of the corresponding equation, Equation 2, confirms the exergonic character of the reaction (Δ_rG^0 = -22.9 KJ mol-1). The value of the standard potential of the nitrobenzyl radical was previously calculated in our group, whereas the standard potential of the nitrobenzyl fluoride anion radical / dianion has been estimated using simulation techniques.



Scheme 16

Equation 2 $\Delta_rG^0 = D_{NO_2PhCH_2X} + F(E^0_1 + E^0{}_2 - E^0_{X^{\cdot}/X^-} - E^0_{NO_2PhCH_2^{\cdot}/NO_2PhCH_2^-}) - T\Delta_rS$

Conclusion

The electrochemical reduction mechanism of the 4-nitrobenzyl iodide (**3**) and 4-nitrobenzyl fluoride (**4**) in polar aprotic solvents has been disclosed using cyclic voltammetry and controlled potential electrolysis.

The electrochemical studies based on the reduction of 4-nitrobenzyl iodide (**3**) reveals a one electron irreversible reduction, which means that the radical anion formed upon reduction is not stable at cyclic voltammetry time scale. The use altogether of cyclic voltammetry and controlled potential electrolysis experiments allows to establish that the chemical reaction linked to the electron transfer is the rupture of the C-I benzylic bond. After that the 4-nitrobenzyl radical anions is able to outrun the radical-radical dimerization.

On the other hand, 4-nitrobenzyl fluoride (**4**) shows a different behavior respect to the **3.** Compound **4** undergoes one electron reversible electron transfer (E^o=-1.02 vs. SCE), which means that the radical anion is stable at cyclic voltammetry time scale. This first electron transfer is followed by a second electron transfer at Epc=-1.71 vs. SCE at 0.5 V s^{-1}. Since the reduction wave is irreversible, it is possible to conclude that there is a chemical reaction linked to the electron transfer. The use of cyclic voltammetry and controlled potential electrolysis permits to establish that the C-F bond cleavage is the chemical reaction coupled to this second electron transfer.

The calculation of $\Delta_r G^0$ for the bond breaking reaction of C-I and C-F supports the fact that the cleavage of the C-I bond is occurring at the first electron transfer, whereas the rupture of the C-F is taking place at the dianion level.

Finally, it has been experimentally observed that the electrolysis of **4** after the first electron transfer, leads to dimeric compounds. The fact that the reaction is endergonic indicates that the C-F bond rupture after the first electron transfer is an unfavorable reaction. Thus, the formation of the dimeric should follow an spontaneous reaction, which can be a dimerisation reaction of to radical anions followed by a loss of two fluoride anions (Scheme 11, path b)

From a synthetic point of view, the radical-radical dimerisation or anion radical dimerisation from the electrogenerated radicals or anion radicals can be relevant for the design of new environmentally friendly methods for obtaining nitroaromatic dimeric compounds.

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